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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,869	10/12/2005	Anders Lehmann	5999-0517PUS1	3025

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

MAIL DATE	DELIVERY MODE
12/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,869	LEHMANN ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-28* is/are pending in the application.

4a) Of the above claim(s) *19-23,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18, 24, 25, 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Amendment filed October 16, 2007 is acknowledged. Claims 15-28 are pending.

In the last Office Action, in response to a Restriction Requirement, Applicants elected Group I, drawn to methods for inhibiting transient lower esophageal sphincter relaxations (TLESRs), for the treatment of GERD, for the prevention of reflux, for the treatment or prevention of regurgitation comprising administering a metabotropic glutamate receptor 5 antagonist. Further, Applicants elected the single species 2-methyl-6-(phenylethynyl)-pyridine (MPEP). Traversals were on the grounds that in Applicants view, the present application relates to a single general inventive concept by reciting a corresponding special technical feature, i.e., the use of an effective amount of a metabotropic glutamate receptor 5 (mGluR5) antagonist, regardless of whether or not different organ systems are encompassed by the present claims.

Applicants presently reiterate their traversal and urge the present invention is directed to the use of mGluR5 antagonists for the inhibition of transient lower esophageal sphincter relaxations and for the treatment of GERD.

Applicants' traversal has been addressed in the last Office Action. The prior art teaches metabotropic glutamate receptors have ubiquitous effects. In addition to mediating glutamatergic synaptic transmission by acting at ionotropic receptors, glutamate also activates a family of G-protein-coupled receptors that modulate neuronal excitability and synaptic transmission. See Martin et al., Neurogastroenterology & Motility Conference (2001). Further, in view of the sensitivity or specificity of said receptors, and the various functionalities

encompassed among those compounds that are deemed to be metabotropic glutamate receptor 5 (mGluR5) antagonists, an undue search burden is presented to the Examiner.

The Restriction Requirement and Election of Species Requirement are still deemed proper and are adhered to. The FINALITY of the Requirements is reiterated.

The subject matter under consideration remains those methods of treatment drawn to inhibiting transient lower esophageal sphincter relaxations (TLESRs), treating GERD, preventing reflux, treating or preventing regurgitation comprising administering the metabotropic glutamate receptor 5 antagonist, 2-methyl-6-(phenylethynyl)-pyridine (MPEP), claims 15-18, 24, 25 and 28.

Those methods drawn to other treatments, as well as the administration of metabotropic glutamate receptor 5 antagonists other than 2-methyl-6-(phenylethynyl)-pyridine, claims 19-23, 26 and 27, remain withdrawn from consideration by the Examiner, as drawn to non-elected inventions, 37 CFR 1.142(b).

Claims 17, 18, 24, 25 and 28 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to the prevention of reflux and the prevention of regurgitation. The specification provides no support for prevention of these conditions. The metabotropic glutamate receptor 5 antagonists MPEP and 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1, 2, 4-oxadiazol-5-yl]benzonitrile, disclosed in Examples 1-3, pages 10-13 of the specification, are shown to inhibit lower esophageal sphincter relaxations (TLESRs) by a percentage.

The instant specification fails to provide guidance that would allow the skilled

artisan background sufficient to practice the instant invention without resorting to undue experimentation.

Applicants argue inhibiting TLESRs would result in prevention of GERD because TLESRs is the dominant cause of GERD. Further, Applicants cite a publication by Holloway et al. that had been listed in an Information Disclosure Statement filed June 28, 2007.

While it is well established that TLESRs is a dominant characteristic of GERD, the term "prevent" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". Applicants have failed to provide guidance as to which particular compound would be preferred for preventing reflux or preventing regurgitation comprising administering a metabotropic glutamate receptor 5 antagonist. The characterization of a particular compound as a metabotropic glutamate receptor 5 antagonist does not presage efficacy for preventing reflux or preventing regurgitation in view of the diverse functionalities of the compounds of the instant claims. The prior art does not recognize metabotropic glutamate receptor 5 antagonist for use in the claimed preventative methods of use.

The rejection of record of claims 17, 18, 24, 25 and 28 under 35 U.S.C. 112, first paragraph, is maintained because the high degree of unpredictability for the prevention of reflux and regurgitation and the lack of guidance provided by the specification would have presented an undue burden to the Examiner.

In the last Office Action claims 15-18, 24, 25 and 28 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It was asserted the claims contain subject matter, that was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The claims recite inhibiting transient lower esophageal sphincter relaxations (TLESRs), treating GERD, preventing reflux, treating or preventing regurgitation comprising administering the metabotropic glutamate receptor 5 antagonist. Passages from The Merck Index were provided to show **various and unrelated etiologic factors may cause** or be the result of TLESRs. Even though GERD is the result of incompetence of the lower esophageal sphincter, variations in intrinsic sphincter pressure, the presence or absence of an inflammatory process, the angle of the cardio-esophageal junction, the action of the diaphragm, the effect of gravity, the volume of gastric contents, local mucosal protective functions and the general health status of the patient must be considered. As required by instant claim 18, a nexus between inhibition of TLESRs and a condition of passively spitting up gastric contents is absent. Further, it is unclear whether conditions of psychogenic vomiting and a correlation to inhibition of TLESRs are contemplated by the present claim language.

Applicants argue a new method for treating GERD is to use mGluR5 antagonists for the inhibition of TLESRs. Applicants urge, based on the "information in the present applicant, a person skilled in the art would be able to conclude that all mGluR5 antagonists would be effective."

Applicants' arguments are not found persuasive because while the Tables on page 11 demonstrate a percent inhibition of TLESRs in an animal model following the administration of MPEP or 3-fluoro-5-[3-(5-fluoropyridin-2-yl)-1-, 2,4-oxadiazol-5-yl]benzonitrile, there is inadequate written disclosure directed to various pathologies that are characterized by "reflux,"

that may or may not be of a gastroesophageal origin, "regurgitation," that may or may not be limited to a pediatric population, and transient lower esophageal sphincter relaxations, which **the prior art recognizes as caused by unrelated, or etiologically distinct, factors**.

Because Applicants have not conveyed possession of the invention with reasonable clarity to one skilled in the art, particularly with respect to dosing regimens that would be required as, particularly, in the case of regurgitation in an infant, or in the case of psychogenic vomiting, the rejection of record of claims 15-18, 24, 25 and 28 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is maintained.

The disclosure lacks sufficient written description for all claimed limitations. An embodiment that meets all the limitations of the claims and sufficient guidance to support predictable operability of the invention to one of ordinary skill in the art are absent.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the Advisory Action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

December 20, 2007